REMARKS

Claims 88-98 are pending. Claims 1-87 are cancelled. Claim 88 has been amended. No new matter has been introduced by the present amendment nor does the amendment require the Office to conduct further searching. Entry of the amendment and reconsideration of the present case in view of the amendment and comments below is respectfully requested.

Interview

Applicants and their representative thank the Examiner and his Supervisor for the courtesy shown during the personal interview conducted on August 15, 2005. The utility rejections and the prior art rejections were discussed and the interview summary agreed upon and placed on the record. Applicants and their representative appreciate the time the Examiner and his Supervisor took to discuss the issues in the present case.

The Claims are Useful

Claims 88-98 were rejected under 35 U.S.C. §§ 101 and 112 because the claimed invention allegedly is not supported by a specific and substantial asserted utility or a well-established utility. Applicants respectfully traverse this rejection.

Applicants have provided sufficient evidence to support the asserted utility

The Office alleged in the final Office Action that the present case is analogous to *Brenner v. Manson*, 383 U.S. 519 (1966). While Applicants agree that the starting point for a utility analysis is *Brenner v. Manson*, that point is the beginning and the end of the relevance of *Manson* to the present case. In *Manson,* the inventor has sought to patent a method for producing a novel hormone, whose sole utility was its potential role as an object of use-testing. Manson disclosed no evidence that the hormone produced by his process had any practical utility. Manson attempted to support the utility asserted in the patent application by pointing to a structurally-related hormone which had been shown to have tumor-inhibiting effects in mice. *Id.* at 531. The Office rejected this assertion indicating that there was an insufficient likelihood that the compound would have the same tumor-inhibiting properties as those related compounds disclosed. *Id.* at 532. "Indeed,

respondent himself recognized that the presumption that adjacent homologues have the same utility has been challenged in the steroid filed because of 'a greater known unpredictability of compounds in that field." *Id.* The facts of the present case stand in stark relief to those of *Manson*.

In the present case, the pending claims are directed to an antibody that specifically binds to a novel protein disclosed in the application. Applicants have asserted in the application that the claimed antibodies have utility as a diagnostic agent to identify prostate and other cancers. Specification, page 5, lines 21-24. The present application contains evidence that the novel gene which encodes the target protein expresses mRNA in prostate cancer cells and not in normal cells, except in normal testis. Specification, page 80, line 25 to page 81, line 2, see also Figure 11. As such, this data is sufficient to support Applicants asserted utility because one of ordinary skill in the art would have a reasonable belief that some protein would be expressed by the mRNA transcripts detected in the target cells. Additionally, Applicants have shown the recombinant expression of the novel protein and the ability to generate antibodies to that protein. See Specification, Example 8, page 88, line 30 to page 92, line 14. This data indicated that the mRNA message detected in the prostate cancer cells contains the predicted open reading frame and encodes a real protein which can serve as an antigen for producing antibodies. All of this data, taken as a whole, is more than sufficient to demonstrate to one of ordinary skill in the relevant art that the presently claimed invention is useful for the detection of prostate cancer.

The Office has not stated a *prima facie* case

When making a rejection for an alleged lack of enablement, the Office must make a *prima facie* showing that the claimed invention lacks utility and it must provide sufficient evidence to support the basis of that *prima facie* showing. *In re Gaubert*, 524 F.2d 1222, 1224 (CCPA 1975); MPEP § 2107.02. The Office alleged that Applicants have not shown definitively that the mRNA expressed in cancer cells is actually translated into protein. The Office further alleged that it is recognized in the art that gene amplification events do not always correlate to increased mRNA or protein expression. The Office further stated that those of ordinary skill in the art recognize that

expression of mRNA does not necessarily correlate or predict protein expression levels. The Office relies upon these assertions to support the *prima facie* showing that the pending claims lack utility.

As evidence to support the *prima facie* showing, the Office cited a number of different publications which were alleged to support the assertion that one of ordinary skill in the relevant art would reasonably doubt that protein is produced from a cancer cell in which mRNA for that protein has been detected. These references include Pennica *et al.*, (1998) *PNAS USA* 95:14717-14722, Konopka *et al.* (1986). *PNAS USA* 83:4049-4052, Haynes *et al.* (1998). *Electrophoresis* 19:1862-1871, Lewin B. (1997). *Genes VI* 29:847-848, and Gokmen-Polar *et al.* (2001). *Cancer Research* 61:1375-1381. These references are reviewed below. As will become readily apparent, none of these references stand for the proposition that one of ordinary skill in the art would reasonably doubt the existence of at least some detectable protein expression occurring when detectable levels of mRNA are present.

The first paper relied upon by the Office is Pennica *et al.* This paper and the one by Konopka *et al.* are cited for the proposition that gene amplification events do not necessarily correlate to increased mRNA levels or to increased protein levels. The utility asserted for the claimed invention does not depend in any way on the issues discussed in the Pennica *et al.* or Konopka *et al.* references. These papers relate to gene amplification events and subsequent mRNA or protein production. Applicants' asserted utility for the claimed invention does not require a gene amplification event. Accordingly, observations regarding gene amplification events and mRNA levels are not relevant to the current discussion. As such, the teachings of the Pennica, *et al.* and Konopka *et al.* references as they relate to gene amplification events do nothing to support the *prima facie* showing advanced by the Office.

Only slightly more relevant to the showing proffered by the Office are the references by Haynes *et al.*, Lewin B., and Gokmen-Polar *et al.* Applicants submit that a careful examination of the data and conclusions of Haynes *et al.* does not support the Office's assertion that detection of a particular mRNA transcript cannot be relied upon for the proposition that protein is expressed from that transcript. As a preliminary matter, applicants note that Haynes *et al.* is a review article. The

data discussed in the Haynes, *et al.* review was subsequently presented in an article by Gygi, *et al.*, *Mol. Cell. Biol.* 19(3):1720-30 (1999). Applicants submit that the teachings of the Gygi, *et al.* reference must be considered in weighing the broad conclusions asserted in the Haynes review and relied upon by the Office. After examining 106 genes with a strikingly similar expression profile to that first reported in the Haynes reference, Gygi *et al.* conclude that there was "a general trend of increased protein levels resulting from increased mRNA levels." *See* Gygi *et al.* at page 1726. In fact, the correlation coefficient for this general trend was 0.935. *See* Gygi *et al.*, Figure 5. Thus, with a rigorous statistical analysis, the correlation between mRNA levels and protein expression was readily apparent. Finally, neither the Haynes review nor Gygi *et al.* provides any evidence or even suggests that elevated levels of a detected mRNA transcript fails to produce any protein expression.

Following the Haynes, *et al.* reference, the Office cited to the Lewin reference for the proposition that control of gene expression can occur at multiple stages and that "production of RNA cannot inevitably be equated with production of protein." The Office has taken this statement quotation out of context. The text of the full quote from Chapter 29 of Lewin at page 847, second column to page 848, first column reads:

> "But having acknowledged that control of gene expression can occur at multiple stages, and that production of RNA cannot inevitably be equated with production of protein, it is clear that the overwhelming majority of regulatory events occur at the initiation of transcription."

Thus, rather than supporting the Office's position, the Lewin citation undermines it. Because the "overwhelming majority" of regulatory events occur during the initiation of transcription and not at the translational level, one of ordinary skill in the art, reading the Lewin reference would reasonably conclude that detection of mRNA is an indication of protein production.

The last reference relied upon by the Office was by Gokmen-Polar, *et al.* This paper discloses a case where there is no increase in mRNA levels but an increase in protein expression. All this paper says is that PKC production in the system studied does not require mRNA overexpression to produce elevated levels of protein. The paper is absolutely silent regarding the

proposition that mRNA can be detected but that there is a reasonable likelihood that no protein will be translated from that mRNA. Accordingly, the Gokmen-Polar, *et al.* paper does nothing to support the position of the Office.

The papers discussed above notwithstanding, the relevant question is at hand is whether one of ordinary skill in the art could reasonably conclude that when mRNA is detected, it is likely that that mRNA is translated into protein which could then be detected by the claimed antibody. The specification has demonstrated that the relevant mRNA is present and differentially expressed in prostate cancer cells and not in normal prostate tissue or in other normal tissues, excluding normal testis. Thus, the claimed antibodies are useful as a diagnostic tool for the detection of prostate cancer. In view of the discussion above, Applicants respectfully submit that the Office has failed to articulate a *prima facie* showing to support the allegation that the pending claims lack a specific, substantial and well-defined utility. As such, Applicants request that the present rejection be withdrawn.

Applicants submit by declaration additional evidence of utility for the claimed invention

In addition to the data provided in the specification and the failure of the Office to articulate a *prima facie* case of obviousness, Applicants submit herewith additional evidence demonstrating that the protein of interest is detectable in tumor samples. This evidence is provided in the form of a Rule 1.132 declaration by Dr. Karen Jane Meyrick Morrison, an employee of the Assignee of the present case.

The data provided in the declaration shows unequivocally that the protein of interest is expressed in prostate cancer and that the protein can be detected by immunochemistry. In addition to prostate cancer, the data provided shows that the protein of interest is also expressed in lung cancer as detected by immunohistochemistry. In view of these showings, it is apparent that 85P1B3 protein can be used to elicit the production of antibodies immunoreactive with 85P1B3 protein, are useful in detecting the presence of cancer.

The claimed invention is useful

The remarks and evidence provided above are sufficient to support Applicants assertion that the claimed subject matter is useful. As such and in view of the fact that the Office has failed to assert a *prima facie* case of lack of utility, Applicants request that the present rejection be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph

Claims 88-98 were rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The Office has alleged that the claims are not enabled for an isolated antibody or fragment thereof that specifically binds to a protein having at least 90% homology to a protein comprising the amino acid sequence disclosed in SEQ ID NO: 728. Without acquiescing to the rejection, Applicants have amended the present claim to delete the homology language. This amendment thus overcomes the reasons given for the present rejection. As such, this rejection should be withdrawn.

Claims 88-98 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection. Nevertheless, in view of the amendment discussed above, the present rejection is now moot as the homology language cited as the basis for the rejection has been deleted. Accordingly, the present rejection should be withdrawn.

Rejection under 35 U.S.C. §102

Claims 88-95 and 97-98 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Tang *et al.* (WO 01/53312). Applicants respectfully traverse this rejection on the grounds that the Tang *et al.* reference is not available as prior art against the presently claimed invention.

The relevant priority date of the Tang *et al.* reference is April 25, 2000

The Tang *et al.* reference is a PCT application (WO 01/53312) published on 26 July 2001, which is after the filing date of the present application. The Tang *et al.* reference claims priority to a number of patent applications filed before the earliest priority of claimed by the present application, specifically, August 28, 2000. The claim for priority in the relevant time period consists of the following applications: 09/488,725 (21 JAN 2000), 09/552,317 (25 APR 2000), 09/598,042 (9 JULY 2000), 09/620,312 (19 JULY 2000) and 09/653,450 (3 AUG 2000).

In making the present rejection, the Office noted that the Tang *et al.* reference disclosed SEQ ID NOs: 3368 and 6940 which are identical to the amino acid sequence of the protein against which the claimed antibody is directed. The Office assumed that the Tang *et al.* reference was entitled to claim the benefit of priority for these sequences all the way back to the earliest priority date recited by the Tang *et al.* reference. However, upon closer examination, this assumption does not withstand scrutiny.

Applicants have attempted to review the disclosures of the various applications relied upon for the Tang *et al.* references priority claim. For example, a copy of the specification for Application No. 09/653,450, filed August 3, 2000 was ordered and inspected. The sequence listing of the 09/653,450 application discloses the presently claimed amino acid sequence as SEQ ID NO: 174.

Application No. 09/620,312 (now U.S. Patent No. 6,569,662), filed July 19, 2000, is available on-line from the U.S. Patent and Trademark Office. A review of the sequence listing of this patent shows that the claimed sequence is not disclosed therein. Accordingly, it appears that the subject matter found in SEQ ID NOS: 3368 and 6940 was added to what would ultimately become the Tang *et al.* reference after this date.

The 09/620,312 application was filed on July 19, 2000 and issued as U.S. Patent No. 6,569,662 and was a continuation-in-part application of U.S. Application No. 09/552,317, filed Apr. 25, 2000, which in turn is a continuation-in-part application of U.S. application Ser. No.

09/488,725, filed Jan. 21, 2000. Presumably if the relevant sequence information was present in any of the early filed cases, it would have also been present in the 09/620,312 application. However, no such reference was found.

Applicants attempted to obtain the file histories of the 09/488,725 and 09/552,317, but were unsuccessful. The sequence listing for the 09/488,725 application was available on-line but did not disclose the relevant sequence. Thus, it is Applicants' position that the Tang *et al.* reference is not entitled to claim priority to a filing date prior to July 19, 2000 for the amino acid sequence at issue. At the in-person interview dated 15-August-2005, Applicants spoke with the Examiner regarding the searching of the sequences. Applicants noted, and the examiner concurred, that upon searching the relevant databases, SEQ ID NO: 3368 is not an amino acid sequence but is disclosed as a 399 base pair polynucleotide from the sequence listing submitted 28-January-2002. In addition, SEQ ID NO: 6940 is not an amino acid but is disclosed as a 1470 base pair polynucleotide from the sequence listing submitted 04-November-2003..

Applicants "swear behind" the Tang *et al.* reference

In the response filed March 17, 2005, Applicants submitted a declaration under 37 CFR § 1.131 which avers that Applicants were in possession of the claimed sequence before the April 25, 2000 filing date of the 09/552,317 application. An applicant for a patent can overcome a reference cited under 35 U.S.C. § 102(e) by the filing of an affidavit or declaration alleging a prior date of invention. 37 CFR § 1.131; M.P.E.P. §§ 715, 2136.05. The declaration must provide evidence of the prior conception, reduction to practice, and diligence during the critical period. 37 CFR § 1.131(b). However, "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show." *In re Stryker*, 58 C.C.P.A. 797, 797 (CCPA 1971). The critical period for which diligence must be shown begins from the time of conception and ends with the invention being reduced to practice. *Mycogen v. Monsanto,* 243 F.3d 1316, 1332 (Fed. Cir. 2001). "In some instances, an inventor is unable to establish a conception until he has reduced the invention to practice through a successful experiment. This situation results in a simultaneous conception and reduction to practice." *Amgen, Inc. v. Chugai Pharmaceutical*

Co., Ltd., 927 F.2d 1200, 1206 (Fed. Cir. 1991). Diligence after the reduction to practice need not be shown. *Ex parte Merz*, 75 USPQ 296, 297 (Bd. App. 1947).

To further support the previously filed 1.131 Declaration Applicants provide a copy of a laboratory notebook page of Dr. Steve Mitchell which indicates that a full length clone obtained by the inventors had the sequence of the protein OIP5. This evidence taken with the declaration of the inventors is sufficient to establish that Applicants had reduced a relevant portion of the claimed invention to practice before April 25, 2000.

The proffered evidence indicates that Applicants had identified the gene of interest, isolating it from a cancer sample, and determining the sequence of the gene prior to the relevant date. As such, the evidence provided in the declaration shows exactly the same amount and quality of evidence of invention as that provided in the Tang *et al.* reference. As such, the showing in declaration satisfies the evidentiary hurdle for Rule 1.131 declarations.

The Office asserted in the Action that Applicants needed to demonstrate the requisite level of diligence in addition to providing sufficient evidence of the actual reduction to practice for the Rule 131 declaration to over come the Tang *et al.* reference. Applicants disagree. In this case, Applicants need not assert diligence from the time of conception until reduction to practice because the present invention was simultaneously conceived and reduced to practice when the clone of the protein recited in the claims was sequenced. Moreover, diligence need not be asserted after the time of the reduction to practice for the purposes of swearing behind a reference.

In view of the relevant priority date established for the Tang *et al.* reference and the Rule 1.131 declaration provided herewith, Applicants submit that the present rejection has been overcome and should be withdrawn.

Rejection under 35 U.S.C. §103

Claims 88-98 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Tang in view of Reiter *et al.* (U.S. Patent 6,261,791 B1). To make out a *prima facie case* of obviousness,

the Office must, *inter alia*, cite one or more references which teach or suggest all the limitations of the claimed invention.

As discussed above, the Tang *et al.* reference is not available as prior art against the pending claims. In view of this, the present rejection stands solely on the Reiter *et al.* reference, which neither teaches nor suggests making antibodies to the recited amino acid sequence. Because the Reiter *et al.* reference cannot support the present obviousness rejection, the Office has failed to articulate a prima facie case. Accordingly, the present rejection has been overcome and should be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 511582002800. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: October 20, 2005

Respectfully submitted,

By _____
James J. Mullen III, Ph.D.
Registration No.: 44,957
MORRISON & FOERSTER LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
(858) 720-7940